nary endothelial dysfunction assessed by cold pressor testing is predictive of long-term cardiovascular event in type 2 diabetic patients with angiographically normal coronary arteries and without other coronary risk factor.

1131-140 Hemodynamic Effects of Aqueous Nitric Oxide Solutions Applied Directly Into Human Coronary Circulation

Malte Kelm, Julius Rath, Petra Kleinbongard, Tienush Rassaf, Michael Preik, Bodo E. Strauer, Universitätsklinikum Düsseldorf, Düsseldorf, Germany

Background: Nitric oxide (NO) has been shown to dilate vessels and to inhibit platelet function, both effects highly desirable during percutaneous intervention (PCI) in patients with coronary artery disease (CAD). Whether or not NO applied directly into human coronary circulation exerts biological effects is unknown so far. Therefore, the aims of our study were: (i) to develop a method for reproducible production of sterile solutions containing authentic NO, (ii) to find a save mode of intracoronary (ic.) application, and (iii) and to characterize potential dilatory effects in conduit and resistance coronary arteries.
Methods: Changes in coronary blood flow (CBF) were quantified by quantitative coronary angiography (QCA) and intracoronary Doppler guide wires (ICD) in 13 patients without flow limiting CAD after application of either saline controls, aqueous NO solutions (NO,1 – 6 µmol), adenosin (ADO, 2.4mg/min) or isosorbiddinitrate (ISDN, 0.3 mg) in random order.
Results: NO dilated epicardial arteries in a dose-dependent manner up to 10±1%, equivalent to that seen upon ISDN. In parallel average peak velocity (APV) increased from 21 to 51+4 cm/s. Thus NO dilated coronary microvasculature to almost the same degree as seen after infusion of adenosine, whereas ISDN increased APV only slightly. Consequently, coronary blood flow increased according to the following rank order: NO and ADO > ISDN, whereas saline controls were without effect. NO induced increases in CBF lasted much longer than expected from its biochemical life span in human blood. Heart rate or blood pressure remained unaffected.
Conclusions: Aqueous NO solutions can be applied directly into human coronary circulation and dilate uniformly epicardial *and* resistance arteries increasing coronary blood flow severalfold. These findings offers the avenue to selectively increase local NO stores within the coronary circulation without exerting systemic side effects.

1131-141 Coronary Endothelial Function: The Impact of Aging in a Matched Study Group With Normal Coronary Arteries

Jan L. Houghton, Patricia Kuhner, Mikhail Torosoff, Michael Prisant, Albany Medical College, Albany, NY

Background: Coronary endothelial vasodilator function is attenuated with aging. It is unknown whether this finding is simply related to greater prevalence of risk factors and/or subclinical atherosclerosis among the elderly or alternatively to a direct or indirect effect of aging. Methods: Using graded coronary infusions of acetylcholine (ACh), endothelial function was tested in 25 patients between the ages of 20 and 45 years (defined as young) and in 25 matched patients aged 60 or older (defined as old). All patients had angiographic normal coronary arteries and were matched for gender, race, body mass index (BMI), indexed left ventricular mass (LVMH), low density lipoprotein cholesterol (LDL-C), and mean arterial pressure. Results: The study included 14 women and 11 men in each of the young and old groups. Age was 38.6 +/- 1.2 years in the young group and 64.6 +/- 0.7 in the old. Both groups were moderately overweight but not obese. Both were normotensive without left ventricular hypertrophy and LDL-C was less than 135 mg/dl in both. Dose response curves relating % increase in coronary blood flow (CBF) to ACh dose were significantly attenuated among the elderly subjects (p=0.013 by ANOVA) despite similar BMI, LVMH, LDL-C, and blood pressure. Peak increase in CBF after ACh was 228 +/- 18% among the young and 162 +/- 23% among the old (p=0.03). After intracoronary adenosine, peak increase in CBF was also depressed among the old (211 +/- 11% vs 173 +/- 16%, p=0.06). Among the young cohort, 16 of 25 (64%) had greater than 200% increase in CBF above baseline after ACh, a finding present in only 6 of 25 (24%) in the old cohort, p=0.01. Conclusion: In a group of patients with normal coronary arteries matched for body habitus, LVMH, LDL-C, and MAP, aging was associated with depression in endothelial and vasomotor function as indicated by CBF responses to ACh and adenosine. Mechanisms consistent with these results include a direct effect of aging and/or the composite effect of multiple low level atherogenic processes over time.

1131-142 The Relationship of Oxidative Stress to Vascular Health in Humans

Salman Ashfaq, Jerome L. Abramson, Steven D. Rhodes, Sean C. Beinart, Claudine Jurkovitz, Jovonne K. Williams, Viola Vaccarino, Arshed A. Quyyumi, William S. Weintraub, David G. Harrison, Emory University, Atlanta, GA

Background: Experimental animal studies have shown an association between oxidative stress and measures of early atherosclerosis. There is, however, considerably less evidence for this association in humans. A measure of lipid peroxidation in the blood, known as Free Oxygen Radical Monitor or FORM, has been shown to be a marker of oxidative stress in humans. We hypothesized that this marker would correlate with other measures of vascular health.
Methods: 40 subjects with no overt atherosclerotic disease were enrolled. As measures of vascular health, ultrasound evaluation of common carotid artery intima media thickness (CIMT), and brachial artery flow mediated dilation (FMD) were performed. FMD is a measure of vascular endothelial function. Plasma levels of high sensitivity C-reactive protein (HsCRP) were also assessed. We correlated these markers with the FORM assay.
Results: There was an inverse correlation between FMD and FORM (r = -0.41, p- 0.01). FORM also had a significant correlation with CIMT (r=0.42, p-0.01). There was also a strong correlation between FORM and HsCRP (r=0.72, p-<0.001). The subjects were also stratified based on their FORM results into those with ≥ 391 and those < 391 Carr Units. The results of the various markers of vascular health are shown below.

	FORM < 391 (Carr Units)	FORM ≥ 391 (Carr Units)	P-value
HsCRP (mg/L)	1.45 (+/-2.5)	6.96 (+/-8.3)	0.01
CIMT (mm)	0.57 (+/-0.10)	0.66 (+/-0.14)	.086
FMD (%)	7.07 (+/-2.5)	4.93 (+/-2.3)	.013

Conclusion: The marker of oxidative stress, FORM, predicts individuals with elevated HsCRP, abnormal endothelial function, and early atherosclerosis. This suggests that it can be used a marker of overall vascular health in humans.

1131-143 Comparison Between the Flow Velocity: Pressure Gradient Relation and the Coronary and Fractional Flow Reserve in the Assessment of Coronary Stenoses

Koen M. Marques, Hugo J. Spruijt, Nico Westerhof, Cees A. Visser, Frans C. Visser, VU University Medical Center, Amsterdam, The Netherlands, ICaR-VU, Amsterdam, The Netherlands

Background. Recently, we assessed the feasibility and reproducibility of the flow velocity - pressure gradient (v-dp) relation. This index involves simultaneous measurement of both the diastolic flow velocity(v) and pressure gradient (dp), giving a comprehensive description of the hemodynamics of a coronary stenosis. The aim of the study was to compare the value of the v-dp relation with the coronary flow velocity reserve (CFVR) and fractional flow reserve (FFR) in the assessment of the severity of a coronary stenosis.
Methods. In all patients a MIBI SPECT or dobutamine stress echocardiogram was performed to detect and locate ischemia. A Doppler and a pressure wire were positioned distal to 90 intermediate coronary stenoses. After administration of adenosine the instantaneous flow velocity, the proximal and distal coronary pressure were digitally recorded. The v-dp relation was computed as described earlier. A ROC curve was used to determine the best cut-off point of the v-dp relation. For the CFVR and FFR the cut-off points 2.0 and 0.75 were used. Sensitivity, specificity, and degree of agreement (kappa) were compared for the three indexes.
Results. The v-dp relation had a higher sensitivity but a lower specificity compared to the FFR. Overall, the v-dp relation was significantly (*p<0.0001) better than the FFR or CFVR to assess the significance of coronary stenoses.
Conclusion. The v-dp relation more accurately predicts the significance of coronary stenoses compared to the CFVR or the FFR.

	CFRV	FFR	v-dp relation
sensitivity	63%	65%	100%
specificity	80%	97%	86%
kappa	0.40±0.07	0.68±0.07	0.76±0.05*

1131-144 Experimental Hyperhomocysteinemia Rapidly Impairs Coronary Flow Velocity Reserve in Healthy Adults

Hiroyuki Takatsu, Hiromi Tasaki, Yoshitaka Nagai, Hiroshi Suzuka, Kazuhito Yamashita, Yasuhide Nakashima, University Occupied Environmental Health, Kitakyushu, Japan

Background: Moderate elevations in plasma homocysteine concentrations are associated with ischemic heart disease. We tested the hypothesis that experimental hyperhomocysteinemia would impair coronary endothelial function by increasing superoxide production. **Methods:** We studied 11 healthy volunteers 23.4 ± 0.9 years of age on average. Coronary flow velocity was measured by transthoracic-Doppler echocardiography before and 4 hours after placebo, oral methionine (L-methionine 0.1g/kg), or oral methionine plus vitamin C (2g), on separate days in random order.
Results: In methionine group, plasma homocysteine level increased from 12.9± 7.0nmol/ml to 32.1± 9.4nmol/ml (p<0.0001), while the averaged diastolic peak velocity under hyperemic conditions (ADPV-hyp) and coronary flow velocity reserve (CFVR) decreased significantly (from 87.2± 11.4cm/sec and 4.1± 0.7 to 75.5± 11.2cm/sec and 3.5 ± 0.5, p=0.0248 and 0.0264, respectively). With simultaneously administration of vitamin C, however, ADPV-hyp and CFVR did not decreased (from 84.4 ± 20.2cm/sec and 3.9 ± 0.86 to 83.3 ± 21.1cm/sec and 3.9 ± 0.87, N.S. and N.S., respectively) in spite of an elevation of the plasma homocysteine level (from 11.7 ± 6.4nmol/ml to 30.6 ± 8.64 nmol/ml, p<0.0001). Moreover, there was a significant negative correlation between plasma homocysteine level and CFVR (r=-0.542, p=0.0092). **Conclusion:** Elevation in homocysteine concentration induced an acute impairment of coronary vessel resistance, and this was completely reverted by vitamin C. Oxidative stress was suggested to play a major role in the deleterious effects of homocysteine on the endothelium of coronary vessels.

1131-145 Differential Antiplatelet Effects of Angiotensin Converting Enzyme Inhibitors: Ex Vivo and In Vitro Studies Using Whole Blood Aggregometry

Dirk Skowasch, Melanie Schneider, Stefanie Schrempf, Stefan Krämer, Mario Maylahn, Gerhard Bauriedel, University of Bonn, Bonn, Germany

Background: Increasing evidence suggests that angiotensin converting enzyme (ACE) inhibitors have antithrombotic effects. Therefore, we sought to evaluate the coagulative ex vivo activity of cardiovascular (CV) patients grouped for treatment with either captopril, ramipril, enalapril, aspirin (ASA) and ASA/clopidogrel or none of these medications and, in addition, the in vitro effects of these ACE inhibitors on platelet aggregation of healthy study participants. **Methods:** Blood samples from 303 CV patients and from 10